AD_____

Award Number: DAMD17-00-1-0033

TITLE: Locating a Prostate Cancer Susceptibility Gene on the X Chromosome by Linkage Disequilibrium Mapping Using Three Founder Populations in Quebec and Switzerland

PRINCIPAL INVESTIGATOR: William D. Foulkes, Ph.D.

CONTRACTING ORGANIZATION: McGill University
Montreal Quebec Canada H3A 2T5

REPORT DATE: March 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	March 2002	Annual (1 Mar 01 - 28 Feb 02)

4. TITLE AND SUBTITLE
Locating a Prostate Cancer Susceptibility Gene on the X Chromosome by Linkage Disequilibrium Mapping Using Three Founder Populations in Quebec and Switzerland

5. FUNDING NUMBERS
DAMD17-00-1-0033

6. AUTHOR(S)
William D. Foulkes, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
McGill University
Montreal Quebec Canada H3A 2T5

E-Mail: william.foulkes@mcgill.ca

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

The funded proposal has not yet been activated at all sites. Approval was given to commence the research at the McGill University hospital site only. IRB approval was obtained from in Switzerland and Chicoutimi and we are working on obtaining the appropriate documents for the final review. Realistically, we anticipate that within the next 6 weeks, we will have obtained the documents needed for approval by Army. Prevalent cases were identified at all McGill University Hospitals (N=497). Treating physicians were contacted to obtain permission to contact their patients. 159 patients were contacted by letter and 93 responses were received. 77 had given consent to participate. 34 pedigrees have been drawn for cases and 3 for controls. 37 cases were shown Ishihara charts and results were recorded. 40 cases and 3 controls have donated their blood and 33 are scheduled to donate blood in the. DNA has been extracted from all blood samples of participants. We are still in the process of contacting patients and extracting DNA as we receive donations from patients. We will be meeting with three physicians who have not yet given permission to contact patients within the next month and will therefore be able to contact the balance of prevalent cases.

14. SUBJECT TERMS
Prostate Cancer

15. NUMBER OF PAGES
8

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Locating a prostate cancer susceptibilty gene on the X chromosome by linkage disequilibrium mapping using three founder populations in Quebec and Switzerland.

Dr William Foulkes

New Investigator Award: DAMD17-00-1-0033

Introduction

In this study, we are funded to precisely localise a prostate cancer susceptibility gene to the X chromosome(Xq) by linkage disequilibrium mapping. We plan to use three founder populations : 1) The French Canadian inhabitants of the Saguenay-Lac St Jean region of Quebec; 2) the Ashkenazi Jewish population of greater Montreal; 3) the population of the Swiss Canton of Valais.

We have chosen these three populations because they have all been shown to contain founder mutations in various disease-associated genes and because they are all accessible to us and have participated in research in the past.

Body of text

Task 1: Case assertainment, contact, consent, interview, DNA extraction and pathology confirmation, years 1-3 (aim to complete in second quarter or year 3).

- Obtain approval for this study from the relevant IRBs and submit appropriate documentation for review to start project at the Chicoutimi and Switzerland sites.

In progress

The goal in Task 1 is well underway for 1 of the 3 sites but human subject research cannot commence at the Chicoutimi or Switzerland sites until approval has been granted. Please see appendix for a full description of how we are working to achieve this goal.

However, some of the items in Task 1 have commenced at the McGill University Hospitals (Quebec)

- Identify all prevalent cases of prostate cancer at hospitals serving the three populations undrer the study: Chicoutimi,McGill University Hospitals(Quebec) and Sion and affliated hopitals, Valais, Switzerland.

This goal was achieved at the McGill University Hospitals. Prevalent cases were identified by contacting the tumor registries and medical records. Medical records were examined to confirm diagnosis of prostate cancer and that the patient is living. 497 prevalent cases were found.

Treating physicians were contacted to ask permission to contact their patients by letter.

Three physicians have not yet given their approval to contact their patients but we are meeting with them in the next month and are confident that they will give their support to the study.

Approximately 32 % of the patients were contacted by letter and 60 % of those patients responses were received.

- Identify incident cases through urology clinics at three centers (Chicoutimi, McGill University, and Sion). Method of contact as for prevalent cases.

  This goal has not yet been achieved at the McGill University Hopsitals, but we estimate commencing this goal in the next three to six months.

- Consent all eligible participants (case n~640)

  77 have given their consent to participate. 16 declined to participate in the study.

- Interview and construct three-generation pedigree for each case and control.

  37 pedigrees have been drawn for cases.

- Show Ishihara charts to cases.

  37 cases have been shown Ishihara charts and the results have been recorded.

- Draw blood from all consenting participants.

40 participants have donated their blood and 33 are scheduled to donate their blood in the next three months.

- Extract DNA locally at each participating center, transfer aliquots of DNA to PI laboratory for quality check and storage.

DNA has been extracted at the McGill University site only. DNA extraction and meeting with consenting patients is ongoing.

- Transfer representative slides and blocks to Montreal for central pathology review (*NB* this will take place after ascertainment as we expect a few cases will be reclassified and subsequently excluded).

This goal has not been achieved yet because approval has not been granted at the other sites.

- Create a central database at the MGHRI.

A central database has not yet been created, as there is no information that has been generated from the other two sites. Once the study commence at the other sites we will establish a central database.

Key Research Accomplishments

- Nil

1. Published Work

We have not yet published any work directly related to this project for reasons that are clear from the text above. However, we have continued to work in prostate cancer genetics. We are currently working woth the ICPCG memebers to study the role of RNAse L gene in hereditary prostate cancer. We expect to submit this work in the next few months.

Conclusions

At the present time, we do not have any scientific data to report. We have used the funds alloted for this grant to start the study at the McGill University Hopsitals and to arrange ethical approval at the Sion and Chicoutimi sites. We hope very much that we will be able to report in the next statement that Task 1 is underway at all sites.

Appendix 1

Log of activities of Task 1 at McGill University and obtaining ethical approval at Sion and Chicoutimi sites.

Abbreviations:
JGH-Sir M.B. David- Jewish General Hospital
MGH-Montreal General Hospital
RVH-Royal Victoria Hospital
MUHC-McGill University Hospital Center
MGHRI-Montreal General Hospital Researcj Institute

Continued working towards getting ethics approval at all sites, March 2001-present.

⇓

Permission to start study at the McGill University site granted in June 2001.

⇓

Faxed and mailed hard copy of SPA from Chicoutimi site with the translation to English to Dr. A Howard on September 5,2001.

⇓

Contacted tumor registry at the JGH to identify all prevalent cases at that hospital that were diagnosed from 1991-2001 on September 6,2001.

⇓

Contacted the tumor registry at the RVH and the MGH to identify all prevalent cases at those hospitals that were diagnosed from 1991-2001 on September 7,2001.

⇓

Examined medical records at the JGH, RVH, and MGH to confirm the patient's vital statistic, treating physician, pathology report, and diagnosis from September 11th to November 16 th ,2001.

⇓

Annexes A-D were sent to translation department to be translated into English on October 17th ,2001.

⇓

Letters were sent to treating physicians to ask their permission to contact patients in November 2001.

⇓

Faxed and mailed hard copies of annexes A-D and the appropriate translations to English from Sion site to Dr.A.Howard on November 16,2001.

⇓

Permission was granted from some physicians and letters were sent to patients to ask for their participation in the study from November 16th to January 2002.

⇓

Blood draws for affected individuals and controls as well as interviews about family medical history started on December 4th and is currently ongoing.

⇓

Pedigrees were drawn for individuals who had given blood and provided medical history.

⇓

In the process of arranging meetings with the remaining physicians that have not yet given their permission to contact patients and anticipate their agreement in March 2002.

⇓

DNA is being extracted from blood taken from controls and affected individuals and is ongoing as we receive more consents.

⇓

Certificate of IRB approval and consent form for Switzerland site, along with the translation to English and the SPA application from the Chicoutimi site was faxed and mailed to Ms Mercy Swatson , February 27,2002.